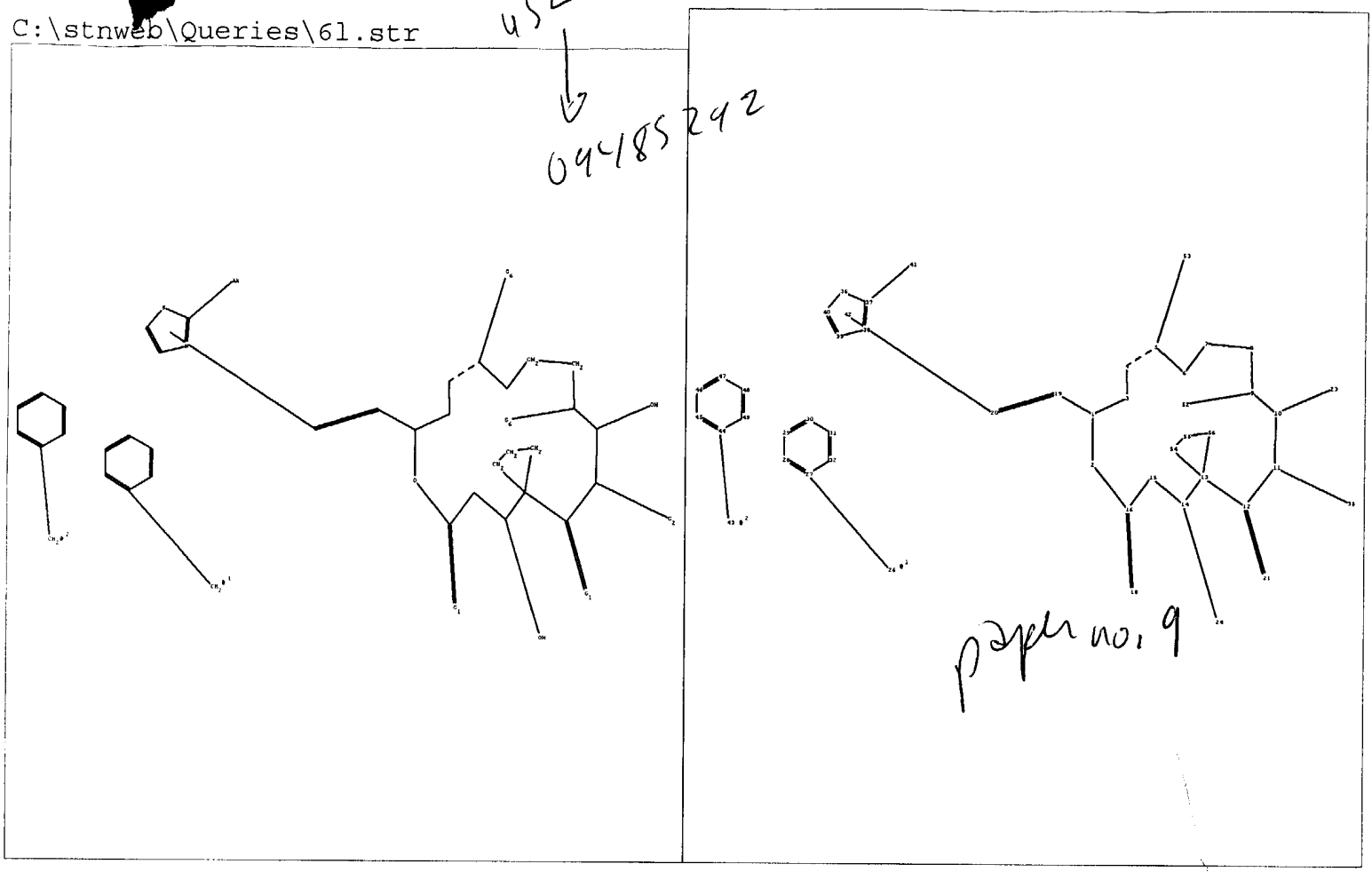
C:\stnweb\Queries\61.str

4526031445 23

09485242



paper no. 9

chain nodes :
18 19 20 21 23 24 26 35 41 43 52 53
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 27 28 29 30 31
32 36 37 38 39 40 44 45 46 47 48 49 54 55 56
chain bonds :
1-19 5-53 9-52 10-23 11-35 12-21 14-24 16-18 19-20 26-27 37-41
43-44
ring bonds :
1-2 1-3 2-16 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13
13-14 13-56 13-54 14-15 15-16 27-28 27-32 28-29 29-30 30-31
31-32 36-37 36-40 37-38 38-39 39-40 44-45 44-49 45-46 46-47
47-48 48-49 54-55 55-56
exact/norm bonds :
4-5 5-6 5-53 9-52 10-23 11-35 12-21 13-56 13-54 14-24 16-18
37-38 37-41 38-39 54-55 55-56
exact bonds :
1-2 1-3 1-19 2-16 3-4 6-7 7-8 8-9 9-10 10-11 11-12 12-13
13-14 14-15 15-16 19-20 26-27 36-37 36-40 39-40 43-44
normalized bonds :
27-28 27-32 28-29 29-30 30-31 31-32 44-45 44-49 45-46 46-47
47-48 48-49
isolated ring systems :
containing 27 : 36 : 44 :

G1:O,S

G2:Ak,Ph,[*1]

G6:Ph,Ak,H,[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 18:CLASS
19:CLASS 20:CLASS 21:CLASS 23:CLASS 24:CLASS 26:CLASS 27:Atom
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 35:CLASS 36:Atom 37:Atom
38:Atom 39:Atom 40:Atom 41:CLASS 42:CLASS 43:CLASS 44:Atom 45:Atom
46:Atom 47:Atom 48:Atom 49:Atom 52:CLASS 53:CLASS 54:CLASS
55:CLASS 56:CLASS

[redacted]

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20	May 17	FRFULL now available on STN

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:55:55 ON 25 MAY 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:56:02 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

```
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   24 MAY 2004  HIGHEST RN 685504-43-2
DICTIONARY FILE UPDATES:  24 MAY 2004  HIGHEST RN 685504-43-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L2       STRUCTURE UPLOADED

=> d 12
L2 HAS NO ANSWERS
L2               STR

=> s 12
SAMPLE SEARCH INITIATED 16:58:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      6 TO ITERATE

100.0% PROCESSED       6 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            6 TO      266
PROJECTED ANSWERS:               1 TO       80

L3             1 SEA SSS SAM L2

=> s 12 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:58:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    152 TO ITERATE

100.0% PROCESSED     152 ITERATIONS                               57 ANSWERS
SEARCH TIME: 00.00.01

L4            57 SEA SSS FUL L2

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                             156.68     156.89

FILE 'HCAPLUS' ENTERED AT 16:58:27 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 25 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l4
L5 8 L4

=> s l5 and klar, u?/au
70 KLAR, U?/AU
L6 7 L5 AND KLAR, U?/AU

=> d l6, ibib abs fhitstr, 1-7

L6 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:693140 HCAPLUS
DOCUMENT NUMBER: 139:191465
TITLE: Use of epothilones in the treatment of brain diseases associated with proliferative processes
INVENTOR(S): Lichtner, Rosemarie; Rotgeri, Andrea; Buchmann, Bernd; Hoffmann, Karin; **Klar, Ulrich**; Schwede, Wolfgang; Skuballa, Werner
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1340498	A1	20030903	EP 2002-4745	20020301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2003074053	A1	20030912	WO 2003-EP2085	20030228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,				

NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004019088 A1 20040129 US 2003-375043 20030228

PRIORITY APPLN. INFO.: EP 2002-4745 A 20020301

US 2002-361062P P 20020301

OTHER SOURCE(S): MARPAT 139:191465

AB The invention provides the use of an epothilone, which shows an av. distribution coeff. between plasma and brain of 0.3-1.5 in the mouse i.v. bolus injection assay, for the prepn. of a medicament for the treatment of a brain disease assocd. with proliferative processes.

IT **289502-84-7**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(epothilones for treatment of brain diseases assocd. with proliferative processes)

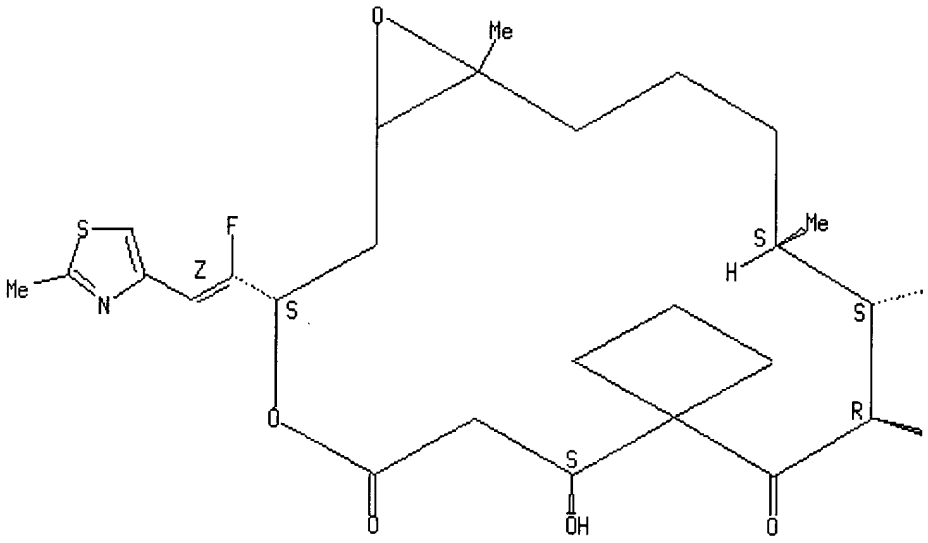
RN 289502-84-7 HCAPLUS

CN Spiro[cyclobutane-1,8'-[4,17]dioxabicyclo[14.1.0]heptadecane]-5',9'-dione, 3'-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-7',11'-dihydroxy-10',12',16'-trimethyl-, (3'S,7'S,10'R,11'S,12'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:790507 HCAPLUS
DOCUMENT NUMBER: 133:362656
TITLE: Preparation of 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilone derivatives and their antitumor activity
INVENTOR(S): **Klar, Ulrich**; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Hoffmann, Jens; Lichtner, Rosemarie
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 298 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066589	A1	20001109	WO 2000-IB657	20000501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19921086	A1	20001102	DE 1999-19921086	19990430
DE 19954228	A1	20010913	DE 1999-19954228	19991104
DE 10015836	A1	20011011	DE 2000-10015836	20000327
BR 2000010190	A	20020108	BR 2000-10190	20000501
EP 1173441	A1	20020123	EP 2000-922826	20000501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002543203	T2	20021217	JP 2000-615619	20000501
EE 200100568	A	20030217	EE 2001-568	20000501
NZ 514989	A	20040227	NZ 2000-514989	20000501

BG 106053	A	20020531	BG 2001-106053		20011026
NO 2001005278	A	20011221	NO 2001-5278		20011029
PRIORITY APPLN. INFO.:			DE 1999-19921086	A1	19990430
			DE 1999-19954228	A1	19991104
			DE 2000-10015836	A1	20000327
			WO 2000-IB657	W	20000501

OTHER SOURCE(S): MARPAT 133:362656
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The antitumor agents, 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilones I (R1a, R1b are same or different = H, C1-C10 alkyl, C6-C12 aryl, C7-C20 aralkyl each optionally substituted; or together = (CH2)m m = 1-5 or -CH2OCH2-; R2a(R2b replace a with b) = H, substituted alkyl, aryl, aralkyl, (CH2)ra-C≡(or =)C-(CH2)pa-R26a, Q, Q1 where n = 0-5; ra, rb = the same or different and = 0-4; pa, pb = the same or different and = 0-3; R3a = H, substituted alkyl, aryl or aralkyl; R3b = OH, OPG14; R14 = H, OR14a, halogen and R14a = H, SO2-alkyl, SO2-aryl or SO2-aralkyl; R4 = H, substituted alkyl, aryl or aralkyl, halogen, OR25, CN; R26a, R26b = same or different = H, substituted alkyl, aryl or aralkyl, C1-C10 acyl or if pa or pb > 0, addnl. a group OR27; R25 = R27 = R22 = H, PG; R5 = H, substituted alkyl, aryl or aralkyl, (CH2)sT s = 1-4, T = OR22 or halogen; R6, R7 = H or together = bond or O; G = X=CR8 or bi- or tricyclic aryl radical and R8 = H, halogen, CN, or substituted alkyl, aryl or aralkyl; X = O, two OR23 groups, C2-C10-alkylene-α,ω-dioxy straight chain or branched; H/OR9 or CR10R11 group and R23 = alkyl radical, R9 = H, PG, R10,R11 = same or different = H, substituted alkyl, aryl or aralkyl, or together with the methylene are a 5-7 carbocyclic ring; D-E = CH2CH2 or OCH2; A = OC(O), OCH2, CH2C(O), NR29C(O), NR29SO2 and R29 = H, alkyl; Z = O or H/OR12 and R12 = H, PG) were prepd. Thus II was prepd. in a multistep synthesis starting from (4S)-4-(2-methyl-1-oxoprop-2-yl)-2,2-dimethyl[1,3]dioxane and 5-trimethylsilylpent-4-in-1-yl magnesium bromide. II had an IC50 value [nM] of 3.0 for the growth inhibition of human MCF-7 breast- and 75 for multidrug resistant NCI/ADR carcinoma cell lines with a selectivity of 2.5. The new epothilone derivs. interact with tubulin by stabilizing microtubuli that are formed. They are able to influence the cell-splitting in a phase-specific manner and are therefore useful in treating diseases or conditions assocd. with the need for cell growth, division and/or proliferation. Thus the epothilone derivs. are suitable for treating malignant tumors, e.g., ovarian, stomach, colon, adeno-, breast, lung, head and neck carcinomas, malignant melanoma, acute lymphocytic and myelocytic leukemia; and for anti-angiogenesis therapy as well as for treatment of chronic inflammatory diseases (such as psoriasis, arthritis).

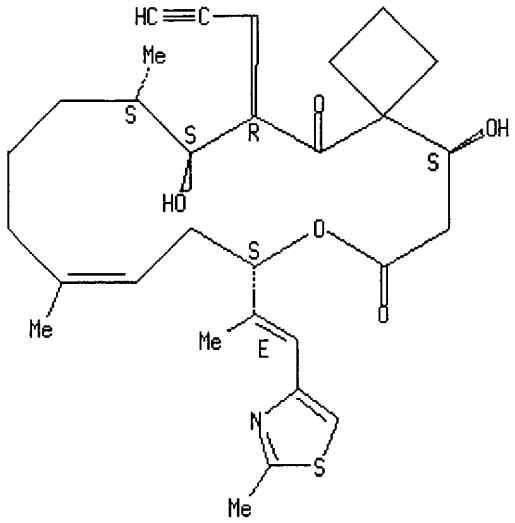
IT **305842-49-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilone derivs. and their use in pharmaceutical prepns.)

RN 305842-49-3 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16-dimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-18-(2-propynyl)-, (5S,9S,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

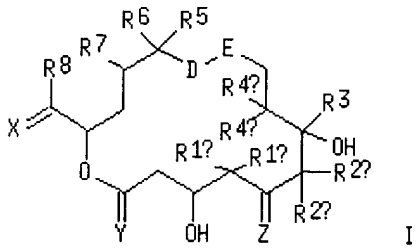
L6 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

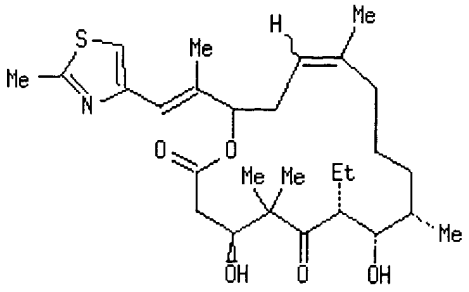
ACCESSION NUMBER: 2000:738730 HCAPLUS
DOCUMENT NUMBER: 133:309795
TITLE: Preparation of new epothilone derivatives and their pharmaceutical uses
INVENTOR(S): **Klar, Ulrich**; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 74 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908767	A1	20001019	DE 1999-19908767	19990218

PRIORITY APPLN. INFO.: DE 1999-19908767 19990218
OTHER SOURCE(S): MARPAT 133:309795
GI



I



II

AB New epothilone derivs. I (R1a,R1b = R2a,R2b = same or different H, alkyl, aryl, aralkyl or (CH2)m,n m, n = 2-5; R3 = H, alkyl, aryl, aralkyl; R4a,R4b = same or different H, alkyl, aryl, aralkyl or (CH2)p = 2-5, CH2CH2, CH=CH, C≡C, epoxy, CH(OH)CH(OH), CH(OH)CH2; D-E = a group; R5 = H, alkyl, aryl, aralkyl; R6,R7 = H, bond, O; R8 = H, alkyl, aryl, aralkyl; X = O, OR23 alkylene-α,-ω-dioxy group straight or branched, OR9 or the CR10R11 group where R23 = alkyl, R9 = H or protecting group and R10,R11 = same or different H, alkyl, aryl, aralkyl or R10,R11 = together with methylene are a 5-7 membered carbocyclic ring; Y = O or two H; Z = O or H/OR12 and R12 = H or a protecting group) were prepd. Thus E- and Z-II were prepd. via a multistep synthesis. I cooperate with tubulin by stabilizing formed microtubuli. I are able phase specifically to affect the cell division and are suitable for the treatment of malignant ovarian, stomach, colon, adeno, breast, lung, head and neck tumors, malignant melanomas, acute lymphocytic and myelocytic leukemia. Derivs. of I are suitable for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). In order to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants I can be applied or incorporated into polymeric materials. I can be used alone or to achieve additive or synergistic effects in combination with further principles and substance classes applicable in tumor therapy.

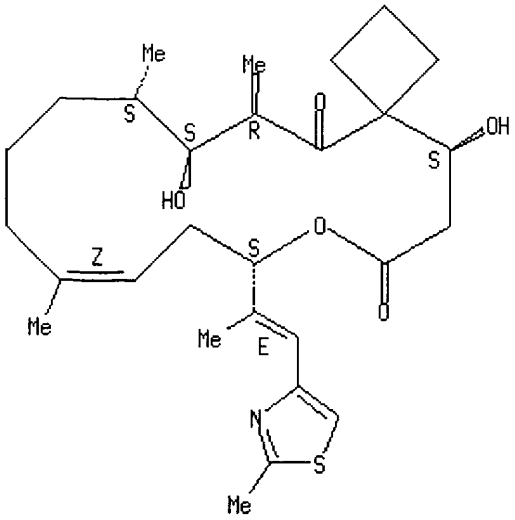
IT **220773-96-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new epothilone derivs. and their pharmaceutical uses)

RN 220773-96-6 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16,18-trimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

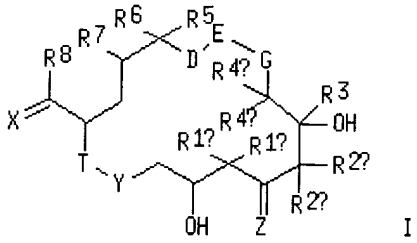
Full Text | Citing References

ACCESSION NUMBER: 2000:592721 HCAPLUS
DOCUMENT NUMBER: 133:193028
TITLE: Preparation of 16-halogen epothilone derivatives and their use as antitumor agents
INVENTOR(S): **Klar, Ulrich**; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Schirner, Michael
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

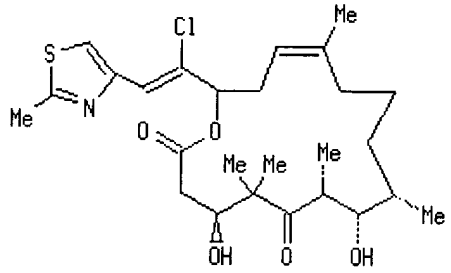
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049021	A2	20000824	WO 2000-EP1333	20000218
WO 2000049021	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19908765	A1	20000824	DE 1999-19908765	19990218
DE 19954230	A1	20011115	DE 1999-19954230	19991104
EP 1150980	A2	20011107	EP 2000-909205	20000218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008331	A	20020129	BR 2000-8331	20000218
JP 2002537301	T2	20021105	JP 2000-599760	20000218
EE 200100431	A	20021216	EE 2001-431	20000218
BG 105802	A	20020329	BG 2001-105802	20010809
NO 2001004013	A	20011018	NO 2001-4013	20010817
ZA 2001007648	A	20030107	ZA 2001-7648	20010917

US 6610736	B1	20030826	US 2001-913495		20011207
US 2004014978	A1	20040122	US 2003-364337		20030212
PRIORITY APPLN. INFO.:			DE 1999-19908765	A	19990218
			DE 1999-19954230	A	19991104
			WO 2000-EP1333	W	20000218
			US 2001-913495	A3	20011207

OTHER SOURCE(S): MARPAT 133:193028
GI



I



II

AB 16-Halogen epothilone derivs. I (R1a, R1b = R2a, R2b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)m m = 2-5; R3 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl; G = O, CH2; R4a, R4b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)p p = 2-5; D-E = 1,2-ethanediyl, 1,2-ethenediyl, ethynyl, oxiranyl, 1,2-dihydroxy-1,2-ethanediyl, 1(2)-hydroxy-1,2-ethanediyl, CH2OH; R5 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, CO2H, CO2-alkyl, CH2OH, CH2O-alkyl, CH2O-acyl, CN, CH2NH2, CH2N(alkyl, acyl)1,2, CH2-halogen; R6, R7 = H, bond, O; R8 = halogen, CN; X = O, two alkoxy groups OR23, C2-C10-alkylene-α,ω-dihydroxy group straight or branched chain, H/OR9, CH10R11 where R23 = C1-C20-alkyl; R9 = H, or protecting group; R10, R11 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, 5-7 membered carbocyclic ring; T-Y = OC(=O), OCH2, CH2C(=O), NR24C(=O), NR24SO2; R24 = H, C1-C10-alkyl; Z = O, H/OR12 where R12 = H or protecting group) were prepd. in addn. to all possible stereoisomers and mixts. Thus II was prepd. from 2-methyl-4-thiazolecarboxaldehyde in a multistep synthesis. The IC50 of II was 5.1 nM on MCF-7 breast tumor and had an IC50 of 37 nM on the multidrug resistant carcinoma NCI/ADR.

IT **289501-46-8P**

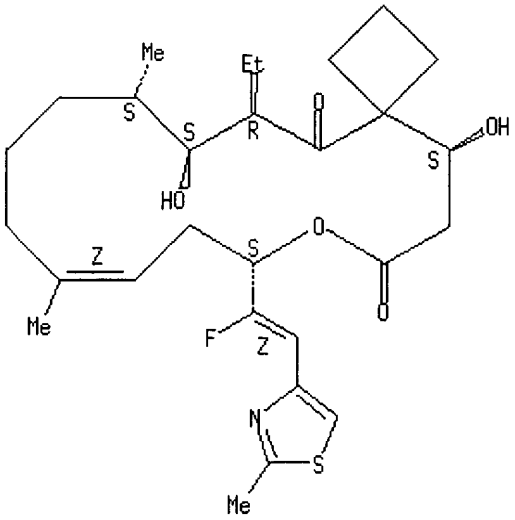
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of 16-halogen epothilone derivs. for use as antitumor agents)

RN 289501-46-8 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 18-ethyl-9-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-5,17-dihydroxy-12,16-dimethyl-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L6 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:573798 HCAPLUS
DOCUMENT NUMBER: 133:177064
TITLE: Preparation of epothilone derivatives useful as pharmaceuticals
INVENTOR(S): **Klar, Ulrich**; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Schirner, Michael
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047584	A2	20000817	WO 2000-EP1104	20000211
WO 2000047584	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19907480	A1	20000817	DE 1999-19907480	19990211
CA 2360952	AA	20000817	CA 2000-2360952	20000211
EP 1161430	A2	20011212	EP 2000-920433	20000211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008206	A	20020219	BR 2000-8206	20000211
JP 2002536450	T2	20021029	JP 2000-598504	20000211
EE 200100422	A	20021216	EE 2001-422	20000211

BG 105803	A	20020329	BG 2001-105803		20010809
NO 2001003900	A	20011011	NO 2001-3900		20010810
ZA 2001007458	A	20021210	ZA 2001-7458		20010910
PRIORITY APPLN. INFO.:			DE 1999-19907480	A	19990211
			DE 1999-19954229	A	19991104
			WO 2000-EP1104	W	20000211

OTHER SOURCE(S): MARPAT 133:177064
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

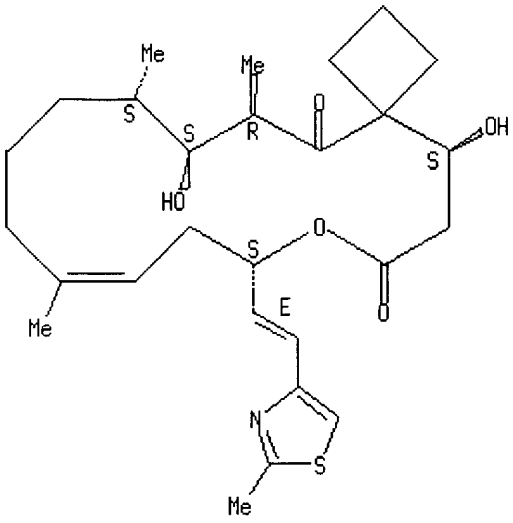
AB Novel epothilone derivs. I (R4 = R5 = H, C1-C10 alkyl, aryl, C7-C20 aralkyl; R6, R7 are each H, or together an addnl. bond or O; R8 = Me or H; R1a, R1b together = trimethylene; R2 = Ph, CH2Ph; X = 2-pyridyl, 2-methyl-4-thiazolyl, 2-methyl-4-oxazolyl; or R1a, R1b together = trimethylene; R2 = Me, Et, Pr; X = 2-pyridyl, 2-methyl-4-thiazolyl, 2-methyl-4-oxazolyl; or simultaneously R1a = R1b = Me; R2 = Me, Et, Pr; X = 2-pyridyl, 2-methyl-4-thiazolyl or 2-methyl-4-oxazolyl; and the N and/or S atoms in X can be in an oxidized form; and if R2 and R8 = Me, X can only be a 2-pyridyl residue which is optionally oxidized at the nitrogen atom) and all possible stereoisomers and their mixts were prepd. Thus II was prepd. in a multistep sequence from the starting materials III and IV. The novel compds. interact with tubulin by stabilizing the formed microtubuli. The compds. are able to influence the cell division in a phase-specific manner and are suited for treating malignant tumors, for example, ovarian cancer, gastric carcinoma, colon cancer, breast cancer, lung cancer, head and neck cancer, malignant melanoma, and acute lymphocytic and myelocytic leukemia. The inventive compds. are suited for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). In order to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants, the inventive compds. can be applied or incorporated in polymeric materials. The inventive compds. can be used alone or, in order to achieve additive or synergistic effects, in conjunction with addnl. constituents and substance classes which can be use in tumor therapy.

IT **288387-10-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epothilone derivs. useful as pharmaceuticals)

RN 288387-10-0 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16,18-trimethyl-9-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,16S,17S,18R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



L6 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:15195 HCAPLUS
DOCUMENT NUMBER: 132:64110
TITLE: The preparation process, intermediate products and pharmaceutical use of epothilone derivatives
INVENTOR(S): Buchmann, Bernd; **Klar, Ulrich**; Skuballa, Werner; Schwede, Wolfgang; Schirner, Michael; Menrad, Andreas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000485	A1	20000106	WO 1999-EP4915	19990630
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19830060	A1	20000210	DE 1998-19830060	19980630
DE 19923001	A1	20001116	DE 1999-19923001	19990513
AU 9950369	A1	20000117	AU 1999-50369	19990630

PRIORITY APPLN. INFO.:
DE 1998-19830060 A 19980630
DE 1999-19923001 A 19990513
WO 1999-EP4915 W 19990630

OTHER SOURCE(S): CASREACT 132:64110; MARPAT 132:64110
GI

NO

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

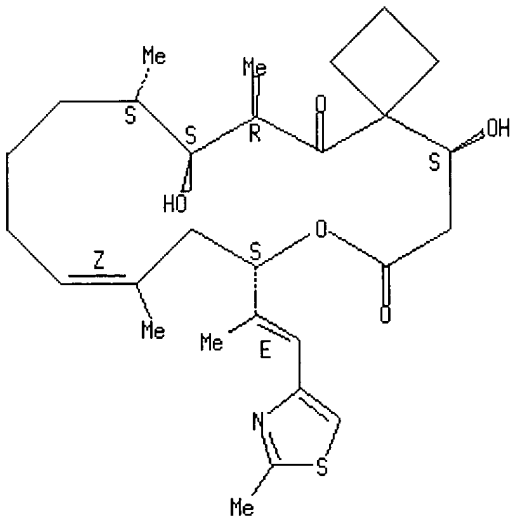
AB The invention relates to new epothilone derivs. I [R1a, R1b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R1aR1b = (CH2)m, m = 2 - 5; R2a, R2b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R2aR2b = (CH2)n, n = 2 - 5; R3 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4a, R4b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4aR4b = (CH2)m, m = 2 - 5; D-E = CH2CH2, CH:CH, C≡C, oxirane ring, CH(OH)CH(OH), CH(OH)CH2; R5 = C1-10-alkyl, aryl, C7-10-aralkyl; R6, R7 = H; R6R7 = O, bond; R8 = C1-10-alkyl, aryl, C7-10-aralkyl; R25 = H, C1-10-alkyl, C1-10-hydroxyalkyl, C1-10-haloalkyl; X = O, (OR9)2, C2-10-alkylene-α,ω-dioxy, CR11R12; CX = CH(OR10); R9 = C1-20-alkyl; R10 = H, protecting group; R11, R12 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R11R12 = CH2, C5-7-carbocyclic ring; Y = O, CY = CH2; CZ = CH(OR13), R13 = H, protecting group] which are prepd. via cyclization of ketones II [R15 = H, OH halogen, OR15a, OSO2R15b; R15a = H, SO2-alkyl, SO2-aryl, SO2-aralkyl, (CH2)o, CR16aR16b; R15b = H, C1-20-alkyl, aryl, C7-20-aralkyl; R16a, R16b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R16aR16b = (CH2)q; o = 2 - 4; q = 3 - 6]. Thus, epothilone deriv. III was prepd. via macrolactonization of carboxylic acid IV with 2,4,6-trichlorobenzoyl chloride and Et3N in THF followed by deprotection with aq. CF3CO2H in CH2Cl2. I cooperate with tubulin by stabilizing formed microtubuli.

IT **253447-53-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and pharmaceutical use of epothilone derivs.)

RN 253447-53-9 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-11,16,18-trimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:126888 HCAPLUS
DOCUMENT NUMBER: 130:196529

TITLE: Preparation of new epothilone derivatives as pharmaceutical agents

INVENTOR(S): **Klar, Ulrich**; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael

PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

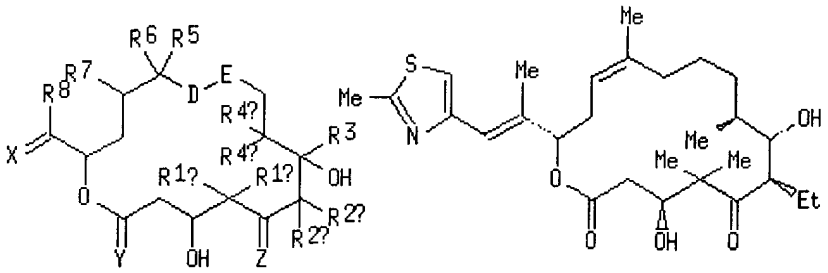
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907692	A2	19990218	WO 1998-EP5064	19980810
WO 9907692	A3	19990514		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19735574	A1	19990211	DE 1997-19735574	19970809
DE 19735575	A1	19990211	DE 1997-19735575	19970809
DE 19735578	A1	19990211	DE 1997-19735578	19970809
DE 19748928	A1	19990429	DE 1997-19748928	19971024
DE 19749717	A1	19990506	DE 1997-19749717	19971031
DE 19751200	A1	19990520	DE 1997-19751200	19971113
DE 19813821	A1	19990923	DE 1998-19813821	19980320
AU 9893409	A1	19990301	AU 1998-93409	19980810
EP 1005465	A2	20000607	EP 1998-946309	19980810
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001512723	T2	20010828	JP 2000-506196	19980810
ZA 9810403	A	20000515	ZA 1998-10403	19981113
US 2003144523	A1	20030731	US 2000-485292	20000503

PRIORITY APPLN. INFO.:

DE 1997-19735574	A	19970809
DE 1997-19735575	A	19970809
DE 1997-19735578	A	19970809
DE 1997-19748928	A	19971024
DE 1997-19749717	A	19971031
DE 1997-19751200	A	19971113
DE 1998-19813821	A	19980320
WO 1998-EP5064	W	19980810

OTHER SOURCE(S): MARPAT 130:196529

GI



I II

AB Epothilone derivs. of formula I [X = O, alkylene-α,ω-dioxy, two alkoxy groups, etc.; Y = O, H2; Z = O, (H, OH), (H, protected OH); R1a, R1b = H, alkyl, aryl, aralkyl, or together = (CH2)m where m = 2, 3, 4, 5; R2a, R2b = H, alkyl, aryl, aralkyl, or together = (CH2)n where n = 2, 3, 4, 5; when D-E = CH2CH2 or when Y = O, R2a or R2b may not be H/Me; R3 = H, alkyl, aryl, aralkyl; R4a, R4b = H, alkyl, aryl, aralkyl, or together = (CH2)p where p = 2, 3, 4, 5; D-E = CH2CH2, CH:CH, C≡C, 2,3-oxiranediyl, CH(OH)CH(OH), CH(OH)CH2; R5 = H, alkyl, aryl, aralkyl; R6, R7 = H, together = a satd. bond or O; R8 = H, alkyl, aryl, aralkyl all of which may be substituted] are prepd. Thus, the title compds. (4S,7R,8S,9S,13E,16S(E))- and (4S,7R,8S,9S,13Z,16S(E))-4,8-dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethylcyclohexadec-13-en-2,6-dione (II) were prepd. in many steps. The new compds. interact with tubulin by stabilizing formed microtubuli. They are capable of influencing cell division in a phase-specific manner and are suitable for the treatment of malignant tumors, such as ovarian, gastric, colon, breast, lung, head and neck carcinoma, adenocarcinoma, malignant melanoma, and acute lymphocytic and myelocytic leukemia. They are also suited for anti-angiogenesis therapy and for the treatment of chronic inflammatory diseases (psoriasis, arthritis). To prevent uncontrolled cell growth on, and for better tolerability of, medical implants, the derivs. can be introduced into or applied to polymeric materials. The compds. provided for in the invention can be used alone or, to achieve additive or synergistic effects, in combination with other principles and substance categories used in tumor therapy.

IT **220773-96-6P**

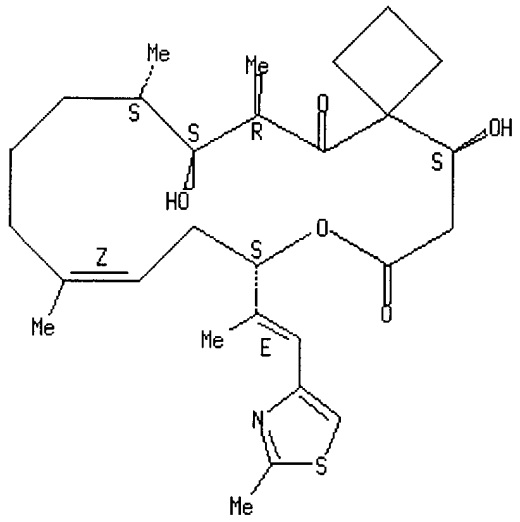
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of epothilone derivs. as antitumor agents)

RN 220773-96-6 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 5,17-dihydroxy-12,16,18-trimethyl-9-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




```
=> file caold
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        35.66     192.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -4.85      -4.85

FILE 'CAOLD' ENTERED AT 16:59:09 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  This file supports REG1stRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

=> d his

     (FILE 'HOME' ENTERED AT 16:55:55 ON 25 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:56:02 ON 25 MAY 2004
L1              STRUCTURE UPLOADED
L2              STRUCTURE UPLOADED
L3            1 S L2
L4           57 S L2 FULL

     FILE 'HCAPLUS' ENTERED AT 16:58:27 ON 25 MAY 2004
L5            8 S L4
```

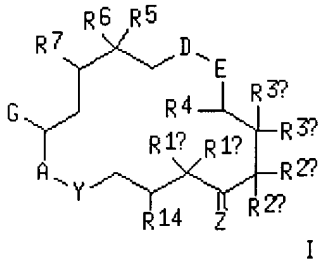
```
L6             7 S L5 AND KLAR, U?/AU

     FILE 'CAOLD' ENTERED AT 16:59:09 ON 25 MAY 2004

=> s l4
L7             0 L4

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.42     192.97

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -4.85

FILE 'HCAPLUS' ENTERED AT 16:59:19 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 25 May 2004  VOL 140 ISS 22
FILE LAST UPDATED: 24 May 2004  (20040524/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l5 not l6
L8             1 L5 NOT L6

=> d l8, ibib abs fhitstr, 1

L8   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

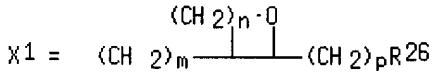
```
ACCESSION NUMBER:          2002:157050  HCAPLUS
DOCUMENT NUMBER:           136:216592
TITLE:                     Procedures for the production of 12,13-
                           cyclopropylepothilone derivatives, as well as for
                           their use in pharmaceutical preparations
PATENT ASSIGNEE(S):        Schering Ag, Germany
SOURCE:                    Ger. Offen., 64 pp.
                           CODEN: GWXXBX
DOCUMENT TYPE:             Patent
LANGUAGE:                  German
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:
```

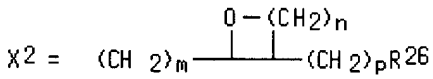
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10041470	A1	20020228	DE 2000-10041470	20000818

PRIORITY APPLN. INFO.: DE 2000-10041470 20000818
OTHER SOURCE(S): CASREACT 136:216592; MARPAT 136:216592
GI



I





AB The present invention describes new 6-alkenyl- and 6-alkynylepothilone derivs., e.g., I [R1a, R1b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R1aR1b = (CH2)r, CH2OCH2; r = 1 - 5; R2a = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)m-C≡C-(CH2)pR26, (CH2)m-C:C-(CH2)pR26, X1, X2; n = 0 - 5; p = 0 - 3; m = 0 - 4; R2b = (CH2)m-C≡C-(CH2)pR26, (CH2)m-C:C-(CH2)pR26, X1, X2; R3a = H, C1-10-alkyl, aryl, C7-20-aralkyl; R3b = O-protecting group; R4 = H, C1-10-alkyl, aryl, C7-20-aralkyl, halogen, OH, O-protecting group, CN; R5 = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)s-T; S = 1 - 4; T = OH, O-protecting group, halogen; R6R7 = C(R33)2, NR32 AY = OC(:O), OCH2, CH2C(:O), NR29C(:O), NR29SO2; DE = CH2CH2, CH2O, OCH2; G = X:CR8-, bicyclic or tricyclic aryl; X = O, (O-alkyl)2, etc.; Z = H, H,OH, H,O-protective group; R8 = H, halogen, CN, C1-20-alkyl, aryl, C7-20-aralkyl; R14 = H, OH, halogen, O-SO2-alkyl, O-SO2-aryl, O-SO2-aralkyl; R26 = H, C1-10-alkyl, aryl, C7-20-aralkyl, C1-10-acyl, OH, O-protecting group; R29 = H, C1-20-alkyl; R32 = H, C1-4-alkyl, C1-4-acyl; R33 = H, halogen], which interact with tubulins by stabilizing the formed microtubulins (no data). I are able specifically to affect cell division and are suitable, for example for the treatment of malignant tumors ovarial -, stomach -, colon -, adeno -, chest -, lungs -, head and neck carcinoma, malignant melanoma, acute lymphocytic and myelocytic leukemia. In addn. I are suitable for the anti-angiogenesis therapy as well as for the treatment of chronic ignitable illnesses (psoriasis, arthritis). For the avoidance of uncontrolled cell rampant growths on as well as the better compatibility of medical implants I can be up and/or brought into polymers materials. According to invention, I can be used alone or for the achievement of additive or synergistic effects in combination with further principles and substance classes applicable in the tumor therapy. Exptl. data from patents PCT/EP00/01333 and PCT/IB00/00657 are reproduced here.

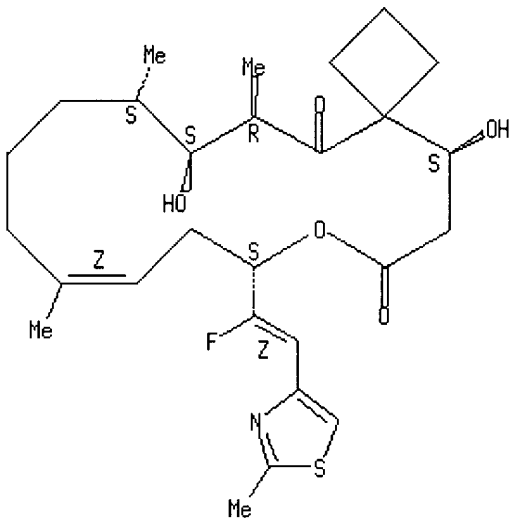
IT **289501-30-0P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 12,13-cyclopropylepothilone derivs. and their use in pharmaceutical compns.)

RN 289501-30-0 HCAPLUS

CN 8-Oxaspiro[3.15]nonadec-11-ene-7,19-dione, 9-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-5,17-dihydroxy-12,16,18-trimethyl-, (5S,9S,11Z,16S,17S,18R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.12	200.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.69	-5.54

FILE 'REGISTRY' ENTERED AT 16:59:35 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2
DICTIONARY FILE UPDATES: 24 MAY 2004 HIGHEST RN 685504-43-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more

```
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L9      STRUCTURE UPLOADED

=> d 19
L9 HAS NO ANSWERS
L9              STR

=> s 19
SAMPLE SEARCH INITIATED 17:03:28 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      1 TO ITERATE

100.0% PROCESSED       1 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               0 TO        0

L10           0 SEA SSS SAM L9

=> s 19
SAMPLE SEARCH INITIATED 17:03:32 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      1 TO ITERATE

100.0% PROCESSED       1 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               0 TO        0

L11           0 SEA SSS SAM L9

=> s 19 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 17:03:38 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     78 TO ITERATE

100.0% PROCESSED      78 ITERATIONS                               33 ANSWERS
SEARCH TIME: 00.00.01

L12          33 SEA SSS FUL L9

=> file hcaplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                157.94     358.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                  0.00      -5.54

FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 25 MAY 2004
```

FILE COVERS 1907 - 25 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s l12
L13           8 L12

=> s l13 and klar, u?/au
             70 KLAR, U?/AU
L14           7 L13 AND KLAR, U?/AU

=> d his

     (FILE 'HOME' ENTERED AT 16:55:55 ON 25 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:56:02 ON 25 MAY 2004
L1               STRUCTURE UPLOADED
L2               STRUCTURE UPLOADED
L3             1 S L2
L4            57 S L2 FULL

     FILE 'HCAPLUS' ENTERED AT 16:58:27 ON 25 MAY 2004
L5             8 S L4
L6             7 S L5 AND KLAR, U?/AU

     FILE 'CAOLD' ENTERED AT 16:59:09 ON 25 MAY 2004
L7             0 S L4

     FILE 'HCAPLUS' ENTERED AT 16:59:19 ON 25 MAY 2004
L8             1 S L5 NOT L6

     FILE 'REGISTRY' ENTERED AT 16:59:35 ON 25 MAY 2004
L9               STRUCTURE UPLOADED
L10            0 S L9
L11            0 S L9
L12           33 S L9 FULL

     FILE 'HCAPLUS' ENTERED AT 17:03:41 ON 25 MAY 2004
L13            8 S L12
L14            7 S L13 AND KLAR, U?/AU

=> s l14 not l6
```

```
L15             0 L14 NOT L6

=>
```